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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,580	09/23/2005	Martin F. Bachmann	1700.0610001/BJD/WBC	8355

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EXAMINER
KINSEY WHITE, NICOLE ERIN

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
04/09/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,580	BACHMANN ET AL.	
	Examiner	Art Unit	
	NICOLE KINSEY WHITE	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *4,6,7,9-11,113,127,129,155,156,158* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☒ Claim(s) *19 and 119* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/20/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,4,6-12,14,15,17,19,21,24,25,35,48,113,115,118-120,122-127,129-131,133-136,139,144-161.

Continuation of Disposition of Claims: Claims rejected are 1,2,8,12,14,15,17,21,24,25,35,48,115,118,120,122-126,130,131,133-136,139,144-154,157 and 159-161.

DETAILED ACTION

Status of the Claims

Claims 155, 156 and 158 are withdrawn from consideration as being directed to a non-elected species.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

It is noted that claim 42 was inadvertently omitted from the listing of rejected claims in the previous rejections under 35 U.S.C. § 103(a). However, the substance of claim 42 (unmethylated CpG-containing oligonucleotides comprising a palindromic sequence can be used to stimulate and enhance an immune response) was addressed

in the previous rejections (see teachings of Krieg et al.). In addition, numerous unmethylated CpG-containing oligonucleotides comprising a palindromic sequence, including SEQ ID NO:1, are well known in the art as evidenced by Carson et al. (WO 97/28259).

Claims 1, 2, 8, 12, 14, 15, 17, 21, 24, 25, 35, 48, 115, 118, 120, 122-126, 130, 131, 133-136, 139, 144-154, 157 and 159-161 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kozlovska et al. (Intervirology, 1996, 39:9-15), Krieg et al. (U.S. Patent Application No. 2003/0050263), Stoll et al. (The Journal of Biological Chemistry, 1977, 252(3):990-993), Bachmann et al. (U.S. Patent Application No. 2003/0099668) and Carson et al. (WO 97/28259).

The claims are directed to a composition comprising:

(a) a virus-like particle;

(b) at least one immunostimulatory substance; and

(c) at least one antigen or antigenic determinant;

wherein said at least one antigen or antigenic determinant is bound to said virus-like particle, and wherein said immunostimulatory substance is packaged into said virus-like particle, and wherein said immunostimulatory substance is an unmethylated CpG-containing oligonucleotide, and wherein said unmethylated CpG-containing oligonucleotide comprises a palindromic sequence, and wherein said palindromic sequence comprises GACGATCGTC (SEQ ID NO: 1), and wherein said antigen comprises at least one HIV polypeptide.

Kozlovska et al. teaches a virus-like particle composed of RNA bacteriophage Qβ capsid proteins fused to HBV preS1 and HIV-1 gp120 V3 epitopes. The capsid proteins and antigens associate through peptide bonds.

Kozlovska et al. does not teach packaging immunostimulatory substances into the Qβ virus-like particles nor SEQ ID NO:10, SEQ ID NO:1 or SEQ ID NO:41. However, Stoll et al. discloses the sequence of the Qβ coat protein (instant SEQ ID NO:10) and Krieg et al. teaches the administration of unmethylated CpG nucleic acids to stimulate and enhance an immune response in a subject to treat HIV. In addition, Krieg et al. teaches that the CpG nucleic acids can be administered using any delivery vehicle known in the art, including virus-like particles (see paragraph [0129]). The CpG nucleic acids of Krieg et al. can contain a palindrome (see paragraph [0025]). Carson et al. discloses recombinant vectors containing immunostimulatory palindromic polynucleotides that are useful for selectively enhancing the TH1 immune response. Carson et al. also discloses instant SEQ ID NO:1 (see pages 61-61 and SEQ ID NO:13 on page 67). Bachmann et al. discloses immunostimulatory nucleic acids such as SEQ ID NO:41 (see Table 1).

Therefore, it would have been obvious to one of ordinary skill in the art to use SEQ ID NO:10 in the virus-like particles of Kozlovska et al. and to modify the virus-like particles of Kozlovska et al. in order to package known immunostimulatory CpG nucleic acids such as those taught by Carson et al. and Bachmann et al. One would have been motivated to do so given the disclosure of SEQ ID NO:10 by Stoll et al., given the suggestion by Krieg et al. that CpG nucleic acids can be delivered in virus-like particles

and that the immunostimulatory CpG nucleic acids can be used to treat HIV, and given the teachings of Carson et al. that instant SEQ ID NO:1 can be used to enhance immune responses. One of ordinary skill in the art would have had a reasonable expectation of success as both components have been used successfully in the art to stimulate and enhance immune responses to antigens and given the fact that viral vectors and virus-like particles (e.g., adenoviral vectors) have been used to deliver nucleic acid and protein antigens.

Further, the courts have said: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose . . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). In this case, applicants are combining two components, virus-like particles carrying antigens and immunostimulatory CpG nucleic acids, which are known in the art to enhance or stimulate an immune response.

With regard to the type of antigen (e.g., cytotoxic epitopes), the number of antigens displayed and the bond types used to join the capsid proteins and the antigen, it is well within the purview of one of ordinary skill in the art to pick and choose the number of antigens to display on the virus-like particle and the method of joining the

antigen(s) to the capsid proteins (e.g., peptide bonds, nonpeptide bonds, other covalent bonds, linkers, etc.).

Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 8, 12, 14, 15, 17, 21, 24, 25, 35, 48, 115, 118, 120, 122-126, 130, 131, 133-136, 139, 144-154, 157 and 159-161 are rejected under 35 U.S.C. 103(a) as being unpatentable over Renner et al. (WO 02/056905) and Krieg et al. (U.S. Patent Application No. 2003/0050263), Bachmann et al. (U.S. Patent Application No. 2003/0099668) and Carson et al. (WO 97/28259).

Renner et al. teaches a virus-like particle composed of RNA bacteriophage capsid proteins, e.g., Qβ, fused to various antigens including HIV-1 epitopes. The capsid proteins, e.g., instant SEQ ID NO:10, and antigens associate through peptide bonds.

Renner et al. does not teach packaging immunostimulatory substances into the Qβ virus-like particles nor SEQ ID NO:1 or SEQ ID NO:41. However, Krieg et al. teaches the administration of unmethylated CpG nucleic acids to stimulate and enhance an immune response in a subject to treat HIV. In addition, Krieg et al. teaches that the CpG nucleic acids can be administered using any delivery vehicle known in the art, including virus-like particles (see paragraph [0129]). The CpG nucleic acids of Krieg et al. can contain a palindrome (see paragraph [0025]). Carson et al. discloses recombinant vectors containing immunostimulatory palindromic polynucleotides that are

useful for selectively enhancing the TH1 immune response. Carson et al. also discloses instant SEQ ID NO:1 (see pages 61-61 and SEQ ID NO:13 on page 67). Bachmann et al. discloses immunostimulatory nucleic acids such as SEQ ID NO:41 (see Table 1).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the virus-like particles of Renner et al. in order to package known immunostimulatory CpG nucleic acids such as those taught by Carson et al. and Bachmann et al. One would have been motivated to do so given the suggestion by Krieg et al. that CpG nucleic acid can be delivered in virus-like particles and that the immunostimulatory CpG nucleic acids can be used to treat HIV and given the teachings of Carson et al. that instant SEQ ID NO:1 can be used to enhance immune responses. One of ordinary skill in the art would have had a reasonable expectation of success as both components have been used successfully in the art to stimulate and enhance immune responses to antigens and given the fact that viral vectors and virus-like particles (e.g., adenoviral vectors) have been used to deliver nucleic acid and protein antigens.

Further, the courts have said: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose . . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). In this case, applicants are combining two components, virus-like particles carrying

antigens and immunostimulatory CpG nucleic acids, which are known in the art to enhance or stimulate an immune response.

With regard to the type of antigen (e.g., cytotoxic epitopes), the number of antigens displayed and the bond types used to join the capsid proteins and the antigen, it is well within the purview of one of ordinary skill in the art to pick and choose the number of antigens to display on the virus-like particle and the method of joining the antigen(s) to the capsid proteins (e.g., peptide bonds, nonpeptide bonds, other covalent bonds, linkers, etc.).

Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 8, 12, 14, 15, 17, 21, 24, 25, 35, 48, 115, 118, 120, 122-126, 130, 131, 133-136, 139, 144-154, 157 and 159-161 are rejected under 35 U.S.C. 103(a) as being unpatentable over Renner et al. (WO 02/056907) and Krieg et al. (U.S. Patent Application No. 2003/0050263), Bachmann et al. (U.S. Patent Application No. 2003/0099668) and Carson et al. (WO 97/28259).

Renner et al. teaches a virus-like particle composed of RNA bacteriophage capsid proteins, e.g., Qβ, fused to various antigens including HIV-1 epitopes. The capsid proteins, e.g., instant SEQ ID NO:10, and antigens associate through peptide bonds.

Renner et al. does not teach packaging immunostimulatory substances into the Qβ virus-like particles nor SEQ ID NO:1 or SEQ ID NO:41. However, Krieg et al.

teaches the administration of unmethylated CpG nucleic acids to stimulate and enhance an immune response in a subject to treat HIV. In addition, Krieg et al. teaches that the CpG nucleic acids can be administered using any delivery vehicle known in the art, including virus-like particles (see paragraph [0129]). The CpG nucleic acids of Krieg et al. can contain a palindrome (see paragraph [0025]). Carson et al. discloses recombinant vectors containing immunostimulatory palindromic polynucleotides that are useful for selectively enhancing the TH1 immune response. Carson et al. also discloses instant SEQ ID NO:1 (see pages 61-61 and SEQ ID NO:13 on page 67). Bachmann et al. discloses immunostimulatory nucleic acids such as SEQ ID NO:41 (see Table 1).

Therefore, it would have been obvious to one of ordinary skill in the art to modify the virus-like particles of Renner et al. in order to package known immunostimulatory CpG nucleic acids such as those taught by Carson et al. and Bachmann et al. One would have been motivated to do so given the suggestion by Krieg et al. that CpG nucleic acid can be delivered in virus-like particles and that the immunostimulatory CpG nucleic acids can be used to treat HIV and given the teachings of Carson et al. that instant SEQ ID NO:1 can be used to enhance immune responses. One of ordinary skill in the art would have had a reasonable expectation of success as both components have been used successfully in the art to stimulate and enhance immune responses to antigens and given the fact that viral vectors and virus-like particles (e.g., adenoviral vectors) have been used to deliver nucleic acid and protein antigens.

Further, the courts have said: "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose,

in order to form a third composition to be used for the very same purpose . . . . [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations omitted) (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). In this case, applicants are combining two components, virus-like particles carrying antigens and immunostimulatory CpG nucleic acids, which are known in the art to enhance or stimulate an immune response.

With regard to the type of antigen (e.g., cytotoxic epitopes), the number of antigens displayed and the bond types used to join the capsid proteins and the antigen, it is well within the purview of one of ordinary skill in the art to pick and choose the number of antigens to display on the virus-like particle and the method of joining the antigen(s) to the capsid proteins (e.g., peptide bonds, nonpeptide bonds, other covalent bonds, linkers, etc.).

Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 8, 21, 24, 25, 27, 30, 33, 35, 42, 48, 117, 122, 123, 124, 129, 131, 133-135, 139, 140, 142, 143, 145 and 146 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 10, 14-16, 41, 48 and 55 of copending application 10/563,944. Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept. The instant composition claims are obvious over the claims of the copending application because the claims of the copending application have all of the characteristics of the instant composition claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The elected species SEQ ID NOs: 71, 72 and 85 are free of the prior art of record. Claims 19 and 119 are objected to as being dependent upon a rejected base claim, but would be allowable, as they read on the elected species, if rewritten in

independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NICOLE KINSEY WHITE whose telephone number is (571)272-9943. The examiner can normally be reached on Monday through Friday from 9:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Nicole Kinsey White/
Examiner, Art Unit 1648

/Stacy B Chen/
Primary Examiner, Art Unit 1648